WE CLAIM:

1. A method for making a hypermutable bacteria, comprising the step of: introducing into a bacterium a polynucleotide comprising a dominant negative allele of a mismatch repair gene under the control of an inducible transcription regulatory sequence, whereby the cell becomes inducibly hypermutable.

2. The method of claim 1 wherein the mismatch repair gene is MutH from any species.

3. The method of claim 1 wherein the mismatch repair gene is a MutS homolog from any species.

4. The method of claim 1 wherein the mismatch repair gene is a MutL homolog from any species.

5. The method of claim 1 wherein the mismatch repair gene is a MutY homolog from any species.

6. The method of claim 1 wherein the mismatch repair gene is *PMS2*.

7. The method of claim 1 wherein the mismatch repair gene is plant *PMS2*.

8. The method of claim 1 wherein the mismatch repair gene is *MLH1*.

9. The method of claim 1 wherein the mismatch repair gene is *MLH3*.

10. The method of claim 1 wherein the mismatch repair gene is *MSH2*.

11. The method of claim 1 wherein the mismatch repair gene is a *PMSR* or *PMSL* homolog.

12. The method of claim 3 wherein the allele comprises a truncation mutation.

13. The method of claim 4 where the allele comprises a truncation mutation.

14. The method of claim 6 where the allele comprises a truncation mutation.

15. The method of claim 7 where the allele comprises a truncation mutation.

16. The method of claim 4 wherein the allele comprises a truncation mutation at codon 134.

17. The method of claim 6 wherein the allele comprises a truncation mutation at codon 134.

18. A homogeneous composition of cultured, hypermutable, bacteria which comprise a dominant negative allele of a mismatch repair gene under the control of an inducible transcriptional regulatory sequence.

19. The homogeneous composition of claim 18 wherein the mismatch repair gene is a mutL gene or a homolog thereof.

20. The homogeneous composition of claim 18 wherein the mismatch repair gene is *PMS2* or a homolog thereof.

21. The homogeneous composition of claim 18 wherein the mismatch repair gene is *MLH1* or a homolog thereof.

22. The homogeneous composition of claim 18 wherein the mismatch repair gene is *PMSR* or a *PMSR* homolog.

23. The homogeneous composition of claim 18 wherein the mismatch repair gene is mutS or a homolog thereof.

24. The homogeneous composition of claim 18 wherein the mismatch repair gene is eukaryotic.

25. The homogeneous composition of claim 18 wherein the mismatch repair gene is prokaryotic.

26. The homogeneous composition of claim 20 wherein thebacteria comprise a protein which consists of the first 133 amino acids of PMS2.

27. The homogeneous composition of claim 26 wherein the protein is human PMS2.

28. The homogeneous composition of claim 23 comprising a mammalian MutS protein.

29. The homogeneous composition of claim 19 comprising a mammalian MutL protein.

30. The homogeneous composition of claim 19 comprising a eukaryotic MutL protein.

31. The homogeneous composition of claim 23 comprising a protein which consists of a eucaryotic MutS protein.

32. A method for generating a mutation in a gene of interest comprising the steps of:

growing a bacterial culture comprising the gene of interest and a dominant negative allele of a mismatch repair gene under the control of an inducible transcriptional regulatory sequence, wherein the cell is hypermutable;

testing the cell to determine whether the gene of interest harbors a mutation.

33. The method of claim 32 wherein the step of testing comprises analyzing a nucleotide sequence of the gene of interest.

34. The method of claim 32 wherein the step of testing comprises analyzing mRNA transcribed from the gene of interest.

35. The method of claim 32 wherein the step of testing comprises analyzing a protein encoded by the gene of interest.

36. The method of claim 32 wherein the step of testing comprises analyzing a phenotype associated with the gene of interest.

37. The method of claim 32 wherein bacteria in the bacterial culture are made by the process of introducing a polynucleotide comprising a dominant negative allele of a mismatch repair gene into a bacterium, whereby the cell becomes hypermutable.

38. The method of claim 37 wherein the step of testing comprises analyzing the nucleotide sequence from the gene of interest.

39. The method of claim 37 wherein the step of testing comprises analyzing a protein encoded by the gene of interest.

40. The method of claim 37 wherein the step of testing comprises analyzing a phenotype associated with the gene of interest.

41. A method for generating a mutation in a gene of interest comprising the steps of:

growing a bacterium comprising the gene of interest and a dominant negative allele of a mismatch repair gene under the transcriptional control of an inducible regulatory sequence to form a population of mutated bacteria;

cultivating the population of mutated bacteria under trait selection conditions; and

testing at least one of the cultivated bacteria to determine whether the gene of interest harbors a mutation.

42. The method of claim 41 wherein the step of testing comprises analyzing a nucleotide sequence of the gene of interest.

43. The method of claim 41 wherein the step of testing comprises analyzing mRNA transcribed from the gene of interest.

44. The method of claim 41 wherein the step of testing comprises analyzing a protein encoded by the gene of interest.

45. The method of claim 41 wherein the step of testing comprises analyzing a phenotype associated with the gene of interest.

46. The method of claim 41 further comprising the step of growing a cultivated bacteria harboring a mutation in the gene of interest to manufacture a protein produced by said bacteria and harvesting the protein therefrom.

47. The method of claim 41 further comprising the step of growing a cultivated bacteria harboring a mutation in the gene of interest to biotransform a substrate.

48. The method of claim 41 further comprising the step of growing a cultivated bacteria harboring a mutation in the gene of interest to bioremediate.

49. The method of claim 41 wherein the gene of interest is an antibiotic resistance determinant and further comprising the step of comparing the genome of the cultivated bactereia harboring a mutation in the antibiotic resistance determinant to a genome of a corresponding wild type strain, thereby identifying the gene of interest.

50. The method of claim 41 further comprising the step of growing a cultivated bacteria harboring a mutation in the gene of interest to screen effects of a compund library.

51. A method for enhancing the mutation rate of a bacterium, comprising the steps of:

exposing a bacterium comprising a dominant negative allele of an MMR gene to a mutagen whereby the mutation rate of the bacterium is enhanced in excess of the rate in the absence of mutagen and in excess of the rate in the absence of the dominant negative allele.

52.The method of claim 51 wherein the mutagen is a chemical mutagenic agent.

53. The method of claim 51 wherein the mutagen is a DNA alkylating agent.

54. The method of claim 51 wherein the mutagen is a DNA intercalating agent.

55. The method of claim 51 wherein the mutagen is a DNA oxidizing agent.

56. The method of claim 51 wherein the mutagen is ionizing radiation.

57. The method of claim 51 wherein the chemical mutagen is ultraviolet radiation.

58. A method for generating an MMR-proficient bacterium with a new output trait, comprising:

growing a mismatch repair deficient bacterium comprising a defective mismatch repair gene allele and a gene of interest, to form a population of mutated bacteria;

cultivating the population of mutated bacteria under trait selection conditions;

testing at least one of the cultivated bacteria to determine that the gene of interest harbors a mutation; and

restoring mismatch repair activity to the at least one cultivated bacteria.

59. The method of claim 58 wherein the mimatch repair deficient bacterium comprises a dominant negative allele of a mismatch repair gene.

60. The method of claim 59 where in the step of restoring MMR activity comprises removing an inducer chemical that positively regulates the dominant negative MMR allele's expression.

61. The method of claim 59 where in the step of restoring MMR activity comprises excising the dominant negative gene by recombination.

62. The method of claim 59 where in the step of restoring MMR activity comprises knocking out the MMR dominant negative gene allele.

63. The method of claim 59 where in the step of restoring MMR activity comprises negatively selecting for loss of the dominant negative allele from bacterial host.

64. The method of claim 58 wherein the mismatch repair deficient bacterium is treated with a mutagen to enhance the rate of mutation.

65. The method of claim 58 wherein the mismatch repair deficient bacterium is treated with a chemical mutagen to enhance the rate of mutation.

66. The method of claim 58 wherein the mismatch repair deficient bacterium is treated with ionizing radiation to enhance the rate of mutation.

67. The method of claim 58 wherein the mismatch repair deficient bacterium is treated with ultraviolet (UV) irradiation to enhance the rate of mutation.

68. The method of claim 58 wherein the step of restoring MMR activity comprises complementing with a wild-type MMR allele.

69. The method of claim 51 wherein the dominant negative allele is under the control of an inducible promoter.

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70. The method of claim 58 wherein the dominant negative allele is under the control of an inducible promoter.

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